The Examiner has stated that the method of claim 13 is encompassed by the method of claim 12 and that the method of claim 25 is encompassed by the method of claim 24. The claims have been amended to make claim 13 dependent on claim 12 and to make claim 25 dependent on claim 24.

The Examiner has pointed out that claim 15 lacks an antecedent basis. In claim 24 with respect to the term "a phosphorous containing moiety". Claim 14 has been amended to include the term "phosphoramide".

The Examiner has pointed out that claim 21 lacks an antecedent basis in claim 19 upon which it is dependent for "cations". Claim 21 has been amended to depend on claim 20 and therefore provide the proper antecedent basis for the term "cations".

In addition, the Examiner has objected to the use of the Sepharose and Fractosil in claim 9 without the accompanying trademark symbols. Claim 9 has been amended to correct this informality.

1. Rejection of Claims 1-31 Under 35 U.S.C. §112, Second Paragraph

Claims 1-31 of the instant application have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner states that the claims are indefinite and unduly broad because of the expressions "a

polynucleotide of a predetermined sequence" and the term "an initiating substrate". Applicants respectfully traverse this rejection.

The term "polynucleotide of a predetermined sequence" is described at page 30, lines 14-21 of the specification. One of ordinary skill in the art upon reaching that description would understand this term to mean that the order in which the individual nucleotides were added to the initiating substrate using the reactions of the present invention were selected so that when the synthesis is completed, a polynucleotide having a preselected sequence was produced. One of ordinary skill in the art is readily familiar with the concept of a predetermined nucleotide sequence. The predetermined sequence may be any nucleotide sequence as long as it is selected prior to the initiation of the synthesis reaction. In addition, one of ordinary skill in the art understands that a predetermined nucleotide sequence could include a sequence in which a randomly selected nucleotide has been inserted into the sequence at one or more positions within that sequence. One of ordinary skill in the art would recognize that a predetermined nucleotide sequence containing random nucleotides at one or more positions are useful in certain molecular biology procedures. It is therefore respectfully submitted that the term "polynucleotide of a pre-determined sequence" as used in the claims and understood by one of ordinary skill in the art is not indefinite. Applicant respectfully requests that the Examiner withdraw this rejection.

The term "an initiating substrate" is described at pages 14, line 6 - page 17, line 1 of the specification. Specifically, at page 14, lines 9-34, of the specification describes the

requirements for the initiating substrate of the present invention. One of ordinary skill in the art, upon reading this description, would understand the requirements for an initiating substrate in the context of the present invention and claims. In general, initiating substrates contain a nucleoside with a free and unmodified 3'-hydroxyl group. It is at this 3' hydroxyl group that the subsequent addition of nucleotides occurs. The specification describes various embodiments and permutations of useful initiating substrates including, the termini of polynucleotides which are generated using standard molecular biology techniques including the termini of DNA or RNA vectors, single-stranded or double-stranded DNA fragments, single-stranded or double-stranded RNA fragments and RNA or DNA oligonucleotides. The present invention contemplates a variety of initiating substrates each having the required nucleoside with a free and unmodified 3'-hydroxyl group. One of ordinary skill in the art would understand the description of these various initiating substrates provided in the specification. It is therefore respectfully submitted that the Examiner withdraw this rejection.

2. Rejection of Claims 30 and 31 Under 35 U.S.C. § 102(b)

Claims 30 and 31 have been rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Miyoshi et al., (U.S. Patent 4,605,735), Frank et al., (U.S. Patent 4,689,405), and Andrus et al. (U.S. Patents 4,816,571 and 5,047,524). The Examiner states that there is no patentable distinction between the polynucleotides produced by the processes disclosed in Miyoshi, Frank , or Andrus. The applicant respectfully traverses this rejection.

U.S. Patent 4,605,735 to Miyoshi et al. describes a method of preparing polynucleotides which have either biotin or 2,4-dinitrophenyl attached to its 5' end. The polynucleotides produced by Miyoshi et al. are clearly distinguishable from the polynucleotides produced by the present invention. The polynucleotides produced by the present invention do not contain biotin or 2,4-dinitrophenyl attached to the 5' position of the 5'-most nucleotide. Thus, the polynucleotides of the present invention are distinguishable from those of Miyoshi et al.

U.S. Patent 4,689,405 to Frank et al. discloses methods for synthesizing oligonucleotides attached to solid phase supports. Frank et al. disclose attaching nucleotides via the 3' position of a nucleotide to the solid phase support. The polynucleotides of the present invention are clearly distinguishable from the Frank et al. polynucleotides because the process of the present invention produces a polynucleotide attached via its 5' position to the solid support. The remainder of the polynucleotide is then attached to that first nucleotide. Thus, the polynucleotides produced by the methods of the present invention are clearly distinguishable from those of Frank et al.

U.S. Patents 4,816,571 and 5,047,524 to Andrus et al. describe methods for producing polynucleotides on a solid support. The Andrus et al. methods link the 3' position of a nucleotide to a solid support and synthesizing the polynucleotide using the nucleotide which is attached to the solid support as the starting nucleotide. The methods of Andrus et al. produce polynucleotides which are attached via the 3' position of a nucleotide to a solid support. The

Andrus et al. polynucleotides are thus clearly distinguishable from the polynucleotides produced by the methods of the present invention. When the present invention utilizes a solid support, the oligonucleotide is attached to the solid support via the 5' position of that nucleotide. The polynucleotide is then synthesized using this 5'-attached nucleotide as a starting point. Therefore, the Andrus et al. polynucleotides are clearly distinguishable from those of the present invention.

Based on the above remarks, Miyoshi et al., Frank et al., and both Andrus et al. patents do not anticipate the polynucleotides of the present invention. The processes described in these references and the polynucleotides produced by those processes are distinguishable from those of the present invention in that they produce the polynucleotides in the reverse direction (3' to 5'), produce polynucleotides which have a biotin or 2,4-dinitrophenol moiety attached to the 5' nucleotide, or produce polynucleotides which are attached to a solid support via the 3' position of the 3'-most nucleotide. The present invention does not produce polynucleotides in this manner and the polynucleotides produced do not contain these particular moieties attached to the 5'-most nucleotide or to the 3'-most nucleotide.

Based on the above amendments and remarks, the applicant believes that the present claims are in condition for allowance. Applicant respectfully requests early notification thereof.

Respectfully submitted,

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